REMARKS

Reconsideration of the rejections based upon the foregoing amendments and the following remarks is respectfully requested.

A. Allowable Subject Matter

Applicants would like to thank the Examiner for indicating that claims 2, 3, 7, 8, 13, 14, 18, 19, 27, 28, 32, 33, 41, 44, 45 and 48 contain allowable subject matter.

B. Claims 1, 4-6, 9-12, 15-17 and 20-21 were rejected under 35 U.S.C. §102(b) as being anticipated by Singhal.

Claim 1 specifically requires the steps of "a) applying a signal having an AC component to the blood sample; b) measuring an AC phase angle response to the signal; and c) determining the glucose concentration using the AC phase angle response." It is respectfully submitted that the Singhal reference does not teach or suggest the above-recited elements of Applicants' claim 1.

The methodology taught by Singhal et al. is used to allow for selectivity between sugars that may be present in the sample. By looking at several harmonics in the detection of each sugar, Singhal are able to choose a harmonic that is optimal for one sugar and sub-optimal for the other. Sugar (faradaic) signals appear at several harmonics above the first, while the background (charging current, or noise) signal is concentrated in the first two harmonics. The response harmonic chosen for the sugar Singhal are interested in is the one with a phase angle response closest to 90°, as this best isolates the analyte signal from the background noise signal. As the optimal phase angle for detection of a particular sugar varies with each harmonic, the optimal response from the other sugar would be a very small signal at the chosen harmonic.

So, Singhal chooses harmonics where the signal:noise is best for one sugar over another. At the same time, they are looking for a harmonic where the phase angle approaches 90°, to minimize background noise.

Therefore, Singhal teaches selection of a response harmonic that is significant for the analyte of interest (and not for analytes that are not to be measured), by identifying harmonics where the background noise signal is minimum and has a phase angle that is 90 degrees out of phase from the analyte signal. Note that the phase angle is only used by Singhal to select the harmonics that will be measured for a particular sugar – phase angle is NOT used to measure the concentration of the analyte. It is therefore respectfully submitted that Applicants' claim 1, which specifically requires the steps of "a) applying a signal having an AC component to the blood sample; b) measuring an AC phase angle response to the signal; and c) determining the glucose concentration using the AC phase angle response" is not shown or suggested by the references of record.

Claims 4-6, 9 and 10 depend from claim 1 and therefore include all of the limitations of claim 1. It is therefore respectfully submitted that claims 4-6, 9 and 10 are allowable over the references of record for at least the same reasons set forth above with respect to claim 1.

Claim 11 specifically requires the steps of "(a) applying a signal having an AC component to the sample; (b) measuring an AC phase angle response to the signal; and (c) determining the glucose concentration based upon the AC phase angle response and a predetermined correlation between the AC phase angle response and the glucose concentration." It is respectfully submitted that, for the same reasons set forth above with respect to claim 1, the Singhal reference does not teach or suggest the above-recited elements of Applicants' claim 11.

Claims 12, 15-17 and 20-21 depend from claim 11 and therefore include all of the limitations of claim 11. It is therefore respectfully submitted that claims 12, 15-17 and 20-21 are allowable over the references of record for at least the same reasons set forth above with respect to claim 11.

C. Claims 36-40, 42-43 and 46-47 were rejected under 35 U.S.C. §102(b) as being anticipated by de Vries.

Claim 36, as amended, specifically requires "applying at least one signal having an AC component to the blood sample, wherein said at least one signal comprises at least two frequencies applied at least partially simultaneously." It is respectfully submitted that the de Vries reference does not teach or suggest the above-recited elements of Applicants' claim 36.

All of the measurements taught in de Vries are made at single frequencies, and this data is used to construct the charts in the drawing figures of de Vries showing the response of the sample over a range of frequencies. Nowhere in de Vries is it taught or suggested that one should apply "at least one signal having an AC component to the blood sample, wherein said at least one signal comprises at least two frequencies applied at least partially simultaneously" as required by Applicant's claim 36. In fact, de Vries teaches away from this by measuring the sample at discreet frequencies over a range of frequencies. It is therefore respectfully submitted that Applicants' claim 36, as amended, is allowable over the references of record.

Claims 37 and 39 have been canceled herein, therefore their rejection under 35 U.S.C. §102(b) is now considered moot.

Claims 38 and 40 depend from claim 36 and therefore include all of the limitations of claim 36. It is therefore respectfully submitted that claims 38 and 40are allowable over the references of record for at least the same reasons set forth above with respect to claim 36.

Claim 42 as amended, specifically requires "determining the hematocrit value based at least in part upon the first phase angle response and the second phase angle response using

$H_{est} = c_0 + c_1\Phi_1 + c_2\Phi_2$

Where: H_{est} is the hematocrit value,

c_0, c_1 and c_2 are constants, and

Φ_1 and Φ_2 are respective AC phase angle responses

to the first and second signals."

It is respectfully submitted that the de Vries reference does not teach or suggest the above-recited elements of Applicants' claim 42.

The above-recited portion of claim 42 is similar to the limitations of claim 41, which was indicated to contain allowable subject matter in the Office Action. de Vries does not teach or suggest adding phase angle responses together in the manner specified by claim 42. It is therefore respectfully submitted that claim 42 is allowable over the references of record.

Claim 43 has been canceled herein, therefore its rejection under 35 U.S.C. §102(b) is now considered moot.

Claim 46, as amended, specifically requires "wherein the first frequency and the second frequency are applied at least partially simultaneously." It is respectfully submitted that the de Vries reference does not teach or suggest the above-recited elements of Applicants' claim 46.

All of the measurements taught in de Vries are made at single frequencies, and this data is used to construct the charts in the drawing figures of de Vries showing the response of the sample over a range of frequencies. Nowhere in de Vries is it taught or suggested that "the first frequency and the second frequency are applied at least partially simultaneously" as required by Applicant's claim 46. In fact, de Vries teaches away from this by measuring the sample at

discreet frequencies over a range of frequencies. It is therefore respectfully submitted that Applicants' claim 46, as amended, is allowable over the references of record.

Claim 47, as amended, specifically requires "wherein the first frequency, the second frequency, the third frequency and the fourth frequency are applied at least partially simultaneously." It is respectfully submitted that the de Vries reference does not teach or suggest the above-recited element of Applicants' claim 47.

All of the measurements taught in de Vries are made at single frequencies, and this data is used to construct the charts in the drawing figures of de Vries showing the response of the sample over a range of frequencies. Nowhere in de Vries is it taught or suggested that "the first frequency and the second frequency are applied at least partially simultaneously" as required by Applicant's claim 47. In fact, de Vries teaches away from this by measuring the sample at discreet frequencies over a range of frequencies. It is therefore respectfully submitted that Applicants' claim 47, as amended, is allowable over the references of record.

D. Claims 22-26, 29-31 and 34-35 were rejected under 35 U.S.C. §103(a) as being obvious in view of Singhal in view of Bodai (US 4,929,426), Doss and de Vries.

Claim 22 specifically requires "(a) applying a signal having an AC component to the sample; (b) measuring an AC phase angle response to the signal; and (c) determining the glucose concentration using the first AC phase angle response and a predetermined compensation factor." It is respectfully submitted that the cited references, when taken alone or in combination, do not teach or suggest the above-recited elements of Applicants' claim 22.

The methodology taught by Singhal et al. is used to allow for selectivity between sugars that may be present in the sample. By looking at several harmonics in the detection of each sugar, Singhal are able to choose a harmonic that is optimal for one sugar and sub-optimal for the

other. Sugar (faradaic) signals appear at several harmonics above the first, while the background (charging current, or noise) signal is concentrated in the first two harmonics. The response harmonic chosen for the sugar Singhal are interested in is the one with a phase angle response closest to 90°, as this best isolates the analyte signal from the background noise signal. As the optimal phase angle for detection of a particular sugar varies with each harmonic, the optimal response from the other sugar would be a very small signal at the chosen harmonic.

So, Singhal chooses harmonics where the signal:noise is best for one sugar over another. At the same time, they are looking for a harmonic where the phase angle approaches 90°, to minimize background noise.

Therefore, Singhal teaches selection of a response harmonic that is significant for the analyte of interest (and not for analytes that are not to be measured), by identifying harmonics where the background noise signal is minimum and has a phase angle that is 90 degrees out of phase from the analyte signal. Note that the phase angle is only used by Singhal to select the harmonics that will be measured for a particular sugar – phase angle is NOT used to measure the concentration of the analyte. None of the other cited references cure this deficiency in Singhal, therefore claim 22 is believed to be allowable over the references of record. However, Applicants offer the following additional reasons why the cited combination does not make the claimed invention obvious.

Bodai teaches away by requiring a separate thermistor and Doss does not teach the measurement of the ambient temperature of a sample under test

The Bodai reference is cited to show that it was recognized in the art that temperature variation is something that needs to be measured and corrected for when measuring blood pH.

However, Bodai actually teaches directly away from the claimed invention by teaching that the temperature of the sample should be measured using a silicon thermistor physically placed next to the measurement electrodes (see Column 10, lines 50-61). The Doss reference also does not teach the measurement of ambient sample temperature using AC excitation, but rather the active heating of a sample using AC excitation and controlling the amount of heating by monitoring the phase shift of the AC signal that is input to the antenna. Furthermore, Doss teaches this effect in a subcutaneous antenna implanted in (phantom) human tissue, not in a blood sample under test that was the subject of testing in Bodai.

Both Doss and de Vries use electrode configurations that are not compatible with Bodai

The implantable antenna of Doss includes electrodes consisting of two parallel rows of cylindrical pins embedded in (phantom) human tissue. These electrodes are coupled to the excitation and measurement electronics using a pair of antennas held in close proximity to one another. The measurement system of de Vries uses a 4 electrode tetrapolar impedance cell to make hematocrit measurements. By contrast, Bodai teaches the use of an electrochemical measurement cell having a two electrode configuration. The Office Action alleges that it would be obvious to incorporate the measurements of Doss and de Vries with the electrochemical measurement cell of Bodai because of "the ability to measure the temperature and hematocrit without providing anything more than the electrodes already present." It is respectfully submitted that nothing in the prior art of record shows that the measurement techniques of Doss and de Vries are usable with the significantly different electrode configurations of Bodai. Furthermore, there is no teaching or suggestion in the prior art, nor an expectation of success, that the techniques used with the Doss parallel cylindrical pins or the de Vries tetrapolar

impedance cell could be translated to the two electrode arrangements taught by Bodai. For example, the Doss electrode configuration, arrangement and size are important, since they contribute to the measured resistance, and the disclosed electrode arrangement bears no similarity to any of the electrodes taught by Bodai. Similarly, de Vries teaches that "[t]o guarantee a homogeneous electrical field distribution, the distance between the electrodes (10mm) was chosen to be more than twice the radius of the conductivity cell (4mm)" (de Vries, p.466). This is significantly larger than the electrode size of electrochemical blood glucose biosensors of the type taught by Bodai, and the blood sample volumes used by such biosensors would not cover a four electrode configuration of this scale.

It is not obvious to use DC and AC in a test using reagents

The biosensors of Bodai all comprise electrochemical cells that use DC signals to test for analytes, wherein the DC responses are generated via reactions (usually enzymatic) that require reagents. The AC signal responses detected by Doss and de Vries are generated directly from the parameters of interest (temperature for Doss and hematocrit for de Vries): they are direct measurements of physical and physico-chemical properties without a specifying reagent. There is no teaching, suggestion or motivation in the art, nor would it be obvious to try, to use both DC signals and signals having an AC component together in the same environment, in the presence of a reagent, and with the same electrodes. It is recognized by Applicants that claim 22 does not require a DC signal or a reagent, but the Bodai reference relates to DC tests conducted in the presence of a reagent, therefore it would not be obvious to use the AC methods of Doss and de Vries, which do not use reagents, with these DC reagent-based tests. Therefore, one skilled in the art would not be motivated to combine the various tests as suggested by the Examiner, and

the combination of references relied upon in the Office Action do not render Applicant's invention obvious.

It is therefore respectfully submitted that Applicants' claim 22, which specifically requires the steps of "a) applying a signal having an AC component to the blood sample; b) measuring an AC phase angle response to the signal; and c) determining the glucose concentration using the AC phase angle response" is not shown or suggested by the references of record.

Claims 23-26, 29-31 and 34-35 depend from claim 22 and therefore include all of the limitations of claim 22. It is therefore respectfully submitted that claims 23-26, 29-31 and 34-35 are allowable over the references of record for at least the same reasons set forth above with respect to claim 22.

E. New Claims 49 and 50

New claim 49 has been added herein generally based upon original claims 36, 44 and 45 and including the limitation "wherein the AC component comprises a frequency between about 1 kHz and about 20 kHz." It is believed that the cited references do not show or teach this element of Applicants' new claim 49, as confirmed by the Examiner's indication that claims 44 and 45 contained allowable subject matter.

New claim 50 has been added herein generally based upon original claims 42, 44 and 45 and including the limitation "the first signal having a first frequency between about 1 kHz and about 20 kHz." It is believed that the cited references do not show or teach this element of Applicants' new claim 50, as confirmed by the Examiner's indication that claims 44 and 45 contained allowable subject matter.

F. Several references listed on Applicant's Information Disclosure Statement were lined through by the Examiner.

As stated in the Office Action, "the IDS submitted by applicant has several listed references lined through. Where it is clear that the reference had a date that was not usable, the reference was not submitted by applicant, a foreign reference was not submitted with a translation or explanation as required or the citation was a duplicate, the references have been lined through. If applicant feels that one or more of these references is particularly relevant to the claimed invention, the reference should be listed in an IDS with the relevance clearly noted."

It is respectfully submitted that Applicants received a return postcard receipt from the Patent Office indicating receipt of 324 references with Applicants' Information Disclosure Statement filed February 10, 2005 (received by the Patent Office on February 14, 2005). There were 324 non-U.S. patent and non-U.S. published patent application references referenced on Applicants IDS's. As the Examiner is no doubt aware, Applicants are not required to submit copies of issued U.S. patents or published U.S. patent applications (see 37 C.F.R. §1.98(a)(2)(ii)). Therefore, copies of all references listed on Applicants' IDS's that were required to be submitted to the Office have been received by the Office. If any of these submitted references were lined through by the Examiner solely because he does not currently have a copy, it is respectfully requested that these references be identified and Applicant will provide a duplicate copy.

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance, and respectfully request such action. Applicants respectfully request

that the Examiner telephone the undersigned attorney for Applicants at 317-634-3456 if the Examiner does not find that all claims are in condition for allowance as presented herein.

Respectfully submitted,

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